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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 09/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/056,284	WEISS ET AL.	
	Examiner	Art Unit	
	Brian S Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *6-10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 11-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/29/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The rejection of claims 1-4 and 11-25 under 35 USC 112, first paragraph, is withdrawn in light of Remarks/Arguments filed March 15, 2004.

2. The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Rosenquist et al. (US 6025369) is not maintained in light of Amendment and Remarks/Arguments filed March 15, 2004.

3. The rejection of claims 1-2 and 4 under 35 U.S.C. 102(b) as being anticipated by Hammock et al. (WO 00/48593) is not maintained in light of Amendment and Remarks/Arguments filed March 15, 2004.

4. The allowability of claim 5 is withdrawn in light of new ground of rejection.

5. Applicant's arguments with respect to claims 1-4 and 11-25 have been considered but are moot in view of the new ground(s) of rejection.

6. By Amendment filed March 15, 2004, claims 1, 15, 16, 17, 21 and 23-25 have been amended and claims 26-27 have been newly added.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-2, 18-20 and 27 rejected under 35 U.S.C. 102(b) as being anticipated by Erikson et al. (WO 00/23060).

Erikson teaches the administration of epoxide hydrolase inhibitor (e.g., N-[4-(5-ethyl-3-pyridin-3-yl-pyrazol-1-yl)-phenyl]-nicotinamide, N-[4-(5-ethyl-3-pyridin-3-yl-pyrazol-1-yl)phenyl]-1-methylindole-2-carboxamide, etc...) to a subject for the treatment of immunological disorder (i.e., chronic and ischemic acute renal insufficiency, arteriosclerosis, atherosclerosis, interstitial nephritis, transplantation, graft versus host disease, etc...). See page 5, lines 1-25 and claims.

Although Erikson is silent about the instant method of "inhibiting the proliferation of vascular smooth muscle cells" or "inhibiting proliferation of cells with inappropriate cell cycle regulation" in a subject, such claimed method must be inherently presented in the prior art method. Since the prior art method of administering the epoxide hydrolase inhibitor to graft patient or renal transplanted patient or atherosclerotic patient (page 2, para. 8 of the specification) would inherently possess the instantly claimed method. Therefore the reference anticipates the claimed invention.

8. Claim 27 is rejected under 35 U.S.C. 102(b) as being anticipated by Hammock et al. (WO 00/48593).

Hammock (WO 00/48593) teaches the administration of epoxide hydrolase inhibitor such as N,N'-dicyclohexyl urea (Table 1 and 4), to a subject for the treatment of inflammation (i.e., adult respiratory distress syndrome, cancer), wherein said epoxide hydrolase inhibitor is administered at a total daily dose from about 0.001 μM/kg to about 100mg/kg body weight of the mammal (claims 1, 10 and 12-15).

Although Hammock (WO 00/48593) is silent about the instant method of inhibiting proliferation of cells with inappropriate cell cycle regulation in a subject, such claimed method must be inherently presented in the prior art method. Especially in light of the dosage amount disclosed in the instant application (page 15, lines 14-18), the prior art method of using epoxide hydrolase inhibitor (i.e., N,N'dicyclohexyl urea) for the treatment of inflammatory diseases would inherently possess the instantly claimed method when it is administered to said subject at the same dosage amount of from about 0.001 μM/kg to about 100mg/kg body weight of the mammal as disclosed in the instant specification. Therefore the reference anticipates the claimed invention.

9. Claims 1-2, and 27 are rejected under 35 U.S.C. 102(e) as being anticipated by Ingraham et al. (US 2003/0022929 A1).

Ingraham teaches the administration of epoxide hydrolase inhibitor represented by Formula I to a subject for the treatment of cardiovascular diseases including atherosclerosis, coronary artery disease, angina, ischemia, ischemic stroke and renal disease (column 2, para. [0006]; column 8, para. [0100])

Although Ingraham is silent about the instant method of "inhibiting the proliferation of vascular smooth muscle cells" or "inhibiting proliferation of cells with inappropriate cell cycle regulation" in a subject, such claimed method must be inherently presented in the prior art method. Since the prior art method of administering the epoxide hydrolase inhibitor to patients having coronary artery disease, atherosclerosis, angina, ischemia, ischemic stroke or renal disease would inherently possess the instantly claimed method. Therefore the reference anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 11-17 and 22-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingraham et al. (US 2003/0022929 A1) in view of Selmon et al. (US 6120516).

The teaching of Ingraham has been discussed in above 102(e) rejection.

Selmon teaches the correlation of atherosclerosis and hypertension, coronary artery disease, angina or heart attacks. The reference discloses, as well-known scientific knowledge in the art, that atherosclerosis is major cause of coronary artery occlusions characterized by deposits of fatty substances, cholesterol, calcium and fibrin within the arterial wall, and the occlusion can manifest itself in hypertension, ischemia, angina, myocardial infarction, stroke or death; and the coronary artery occlusions is routinely treated by performing coronary artery bypass graft surgery (CABG), percutaneous transluminal coronary angioplasty (PTCA), stents, atherectomy and transmyocardial laser revascularization (column 1, lines 21-34).

The teaching of Ingraham differs from the claimed invention in the administration of N-cyclohexyl-N'-dodecyl urea, specifically to a patient who has (had) a heart attack, coronary bypass, angioplasty, a stent in an arterial lumnen or a natural or synthetic vessel engrafted, wherein said CDU can be administered in combination with cis-epoxyeicosatrienoic acids. To incorporate such teaching into the teaching of Ingraham, would have been obvious in view of Selmon who teaches the correlation of atherosclerosis and hypertension, coronary artery disease, angina or heart attacks; and the atherosclerois as the major risk factor for the coronary artery occlusions; and the routine treatment options (e.g., CABG, percutaneous transluminal coronary angioplasty (PTCA), stents, atherectomy and tranmyocardial laser revascularization) available for the coronary artery occlusions in the art.

One having ordinary skill in the art would have expected that the administration of said soluble epoxide hydrolase inhibitors that has been known to be useful in the treatment of atherosclerosis, coronary artery disease, angina, ischemia and ischemic

stroke would provide therapeutic utility in patient who has (had) a heart attack, coronary bypass, angioplasty, a stent in an arterial lumnen or a natural or synthetic vessel engrafted. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

With respect to claims 17, 21 and 25-26,

In addition to the above mentioned teaching of Ingraham, Ingraham teaches that EETs has similar activity as the soluble epoxide hydrolase inhibitors and enhancement of EETs concentration would have a beneficial therapeutic effect in patients where endothelial dysfunction plays a causative role (column 2, para. [0006]-[0008])

The above references in combination make clear that the soluble epoxide hydrolase inhibitor(s) and EETs have similar activity. It is obvious to combine two compositions each of which is taught by prior art to be useful for same purpose; idea of combining them flows logically from their having been individually taught in the prior art. The combination of active ingredient with the same character is merely the additive effect of each individual component.

11. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ingraham et al. (US 2003/0022929 A1).

The teaching of Ingraham has been discussed in above 35 USC 102(e) rejection. In addition to the above mentioned teaching of Ingraham, Ingraham teaches derivatives

of urea and carbamate inhibitors including CDU and DCU as known soluble epoxide hydrolase inhibitor (column 2, para. [0010]).

Although the teaching of Ingraham differs from the claimed invention in the use of CDU, such substitution would have been obvious to a person skilled in the art. One having ordinary skill in the art would have expected that CDU would have similar activity as the compounds of Formula I as soluble epoxide hydrolase inhibitor. One would have been motivated to make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 1-5, 11-24 and 27 are rejected under the judicially created doctrine of double patenting over claims 1-2 of U. S. Patent No. 6693130 B2 or claims 1-9 of U.S. Patent No. 6531506.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly required "inhibiting the proliferation of vascular smooth muscle cells" would have been inherently presented in the prior art method. Especially in light of the dosage amount disclosed in the instant application (page 15, lines 14-18), the prior art method of using epoxide hydrolase inhibitor (i.e., N,N'dicyclohexyl urea) for the treatment of hypertension would inherently possess the instantly claimed method when it is administered to said subject at the same dosage amount of from about 0.001 μM/kg to about 100mg/kg body weight of the mammal as disclosed in the instant specification. Therefore the reference anticipates the claimed invention.

Although the instant claims limit the recipient of the claimed invention to a subject "(a) has had a heart attack, (b) has had a coronary bypass, (c) has been diagnosed with decreased circulation to the heart, (d) has undergone angioplasty, (e) has an endovascular stent, (f) has a hemodialysis graft, or (g) has a vascular graft", such determination of suitable treatment recipient group would have been obvious to the skilled artisan. For example, hypertension is the most important risk factor for heart attack, and many of patients suffering from heart attack or has had a heart attack are having hypertension.

Conclusion

13. No Claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (571) 272-0951. The fax number for this Group is (703) 872-9306.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Brian Kwon
Patent Examiner
AU 1614